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TITLE: New nitrooxy derivatives used for
treating epilepsy

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PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE
WO 03000643 A1	January 3, 2003	EN
AU 2002314157 A1	January 8, 2003	EN
IT 1325658 B	December 13, 2004	IT

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APPLICATION-DATA:

PUB-NO	APPL-DESCRIPTOR	APPL-NO	APPL-DATE
WO2003000643A1	N/A	2002WO-EP06389	June 11, 2002
IT 1325658B	N/A	2001IT-MI1307	June 21, 2001
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INT-CL-CURRENT:

TYPE	IPC DATE
CIPS	C07C203/04 20060101
CIPS	C07C229/08 20060101
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CIPS	C07C327/34 20060101
CIPS	C07C335/08 20060101
CIPS	C07D213/30 20060101

ABSTRACTED-PUB-NO: WO 03000643 A1**BASIC-ABSTRACT:**

NOVELTY - Nitrooxy derivatives (I) are new.

DESCRIPTION - Nitrooxy derivatives of formula A-(B) ba-(C1)ca-NO₂ (I) and their salts are new.

ba, ca = 0 or 1 (preferably 1);

A = R-T1;

R = a radical of a precursor drug of formula R2-W
(R1)(R0)-(CH2)m;

W = C or N;

R0 = H or (CH2)n-NHR1a;

m, n = 0-2;

R1a = H, C(O)-R1h or C(O)O-R1h;

R1h = U1 or U2;

U1 = 1-10C alkyl, phenyl or benzyl;

U2 = CH(Ry)-NH2, a group of formula (i), C(Ry)(Ry)-
OCORy or 1-methyl-1,2,3,6-tetrahydro-pyridin-4yl;

Ry = H or U1;

R1 = H or electronic doublet on the nitrogen atom
(free valence);

R2 = U3, U4, U5 or U6, or

R2+R1a+W = 4-10 (preferably 6)C ring;

U3 = phenyl (optionally substituted by halo or at
least one OCH3, CF3 or NO2);

U4 = mono- or di-hydroxy substituted benzyl
(preferably 3-4 di-hydroxy substituted);

U5 = H₂N(C=NH);

U6 = Q-(CH)_{p3}(R₈)-(CH)_{p2}(R₇)-(C)_{p1}((R₆)(R_{6a})_p)-CH(R₅)-CH(R₄) (where optionally one ethylenic unsaturation is between the C atoms in position 1 and 2, or 3 and 4 or 4 and 5);

p, p₁, p₂ = 0 or 1;

p₃ = 0-10;

R₄ = H, 1-6C alkyl or free valence;

R₅ = 1-6C alkyl, 3-6C cycloalkyl, free valence or ORa';

Ra' = 1-6C alkyl (optionally substituted by at least one halo (preferably F)) or U₃;

R₆, R_{6a}, R₇, R₈ = H, methyl or free valence;

Q = H, OH, ORb', 3-6C cycloalkyl, 1-6C alkyl, H₂NC(=NH)NH or H₂NC(=S)NH;

Rb' = 1-6C alkyl (optionally substituted by at least one halo (preferably F)), benzyl, or U₃;

T₁ = (CO)_t or (X)_t';

X = O, S or NR_{1c};

R_{1c} = H or 1-5C alkyl;

B = Tb-X₂-Tb₁;

the precursor compound of B = L-carnosine, anserine, selenocysteine, selenomethionine,

penicillamine, N-acetylpenicillamine, cysteine, N-acetylcysteine, glutathione or their esters (preferably ethyl or isopropyl ester), gallic acid, ferulic acid, gentisic acid, citric acid, caffeic acid, dihydrocaffeic acid, p-cumaric acid, vanillic acid, nordihydroguaiaretic acid, quercetin, catechin, kaempferol, sulfurethyne, ascorbic acid, isoascorbic acid, hydroquinone, gossypol, reductic acid, methoxy hydroquinone, hydroxyhydroquinone, propyl gallate, saccharose, 3,5-di-tertbutyl-4-hydroxy-benzylthio glycolate, p-cumaric alcohol, 4-hydroxy-phenylethylalcohol, coniferyl alcohol, allopurinol, 3,3'-thiodipropionic acid, fumaric acid, dihydroxy maleic acid or edetic acid;

Tb = CO or X;

Tb1 = (CO)tx or (X)txx;

t, t', tx, txx = 0 or 1;

X2 = a bivalent group such that the corresponding of precursor of B has free valences of Tb and Tb1 saturated with OZ, Z or N(ZI)(ZII);

Z, ZI, ZII = H or 1-10 (preferably 1-5)C alkyl;

C1 = Tc-Y;

Tc = CO (when tx = 0) or X (when txx = 0) and ba and ca are 1, or

Tc = CO (when t = 0) or X (when t' = 0), or

Tc = CO (when tx = 0) or X (when txx = 0) and ca = 0, tx = 0 and Tb1 = 0;

$Y = Y_p, Y_a \text{ or } Y_{ar};$

$Y_p = (C)_{n1x}(Rt1x)(Rt1x')-Y_3-(C)_{-n11x}(Rt11x)(Rt11x')-O \text{ (ii)};$

$n1x = 0-5 \text{ (preferably 1)};$

$n11x = 1-5 \text{ (preferably 1)};$

$Rt1x, Rt1x', Rt11x, Rt11x' = H \text{ or } 1-4C \text{ alkyl};$

$Y_3 = 5- \text{ or } 6\text{-membered heterocyclyl containing } 1-3 \text{ N, O or S heteroatoms};$

$Y_a = R'O \text{ or } A_a;$

$A_a = (CH_2-CH(ONO_2)-CH_2-O)_{nf'}, (CH_2(ONO_2)-CH(CH_3)-CH_2-O)_{nf'}, (CH(R1f)-CH_2-O)_{nf} \text{ or } (CH_2-CH(R1f)-O)_{nf};$

$R1f = H \text{ or } CH_3;$

$nf' = 1-6 \text{ (preferably } 1-4);$

$nf = 1-6 \text{ (preferably } 2-4);$

$R' = 1-20 \text{ (preferably } 2-6)C \text{ alkyl or } 5-7C \text{ cycloalkylene ring (in which at least one carbon atom is substituted by heteroatoms and the ring can have side chains of } R' \text{ type)};$

$Y_{ar} = Y_{ar1} \text{ or } Y_{ar2};$

$Y_{ar1} = \text{a group of formula (iii)};$

$Y_{ar2} = \text{a group of formula (iv)};$

$n_3 = 0-5, \text{ and}$

$n3' = 1-3,$

provided that:

- (1) ca and ba are not both zero;
- (2) when t is 1, t' is 0 and when t' is 1, t is 0;
- (3) when tx is 1, then txx is 0 and when tx is 0, then txx is 1;
- (4) when W is N , R1 is an electronic doublet on the nitrogen atom (free valence), and
- (5) in (ii), when one unsaturation of ethylene type is present, between carbons 1 and 2, R4 and R5 are free valences to form the double bond between carbons 1 and 2; when the unsaturation is between carbons 3 and 4, R6 and R7 are free valences to form the double bond between carbons 3 and 4; when the unsaturation is between carbons 4 and 5, R7 and R8 are free valences to form the double bond between carbons 4 and 5.

None given in the source material.

USE - Used for treating epilepsy (claimed).

ADVANTAGE - (I) Reduce the incidence and the seriousness of convulsive fits with lower side effects, and show improved activity with respect to the precursor drug in the epilepsy treatment. (I) Can be used in an amount of less than the maximum indicated for the precursor drugs and also at a higher doses considering their very good tolerability.

EQUIVALENT-ABSTRACTS:

ORGANIC CHEMISTRY

Preparation: Preparation of (I) comprises e.g. reacting R-COO-Hal with AgNO₃ to give R-COO-Y-ONO₂ (I').

Preferred Definitions:

Y₃ = pyridine having two free valences in the ortho positions with respect to the nitrogen atom, piperazin-1,4-diyl, 1H-pyrazole (3,5-disubstituted), piperidin-1-yl (where the free valence on the ring is in para position to the nitrogen atom);

B = ferulic acid, N-acetylcysteine, cysteine, caffeic acid, hydro-caffeic or gentisic acid;

R = gabapentine, norvaline, arginine, thiocitrulline, pregabaline, (S)3-isobutyl-gamma aminobutyric acid, agmatine, vigabatrine or 2-amino, (3,4-dihydroxyphenyl)propanoic acid (dopa).

Administration is parenteral, oral or topical (claimed).

Administration is optionally in combination with NO donor compounds containing drugs belonging to the classes of aspirin, ibuprofen, paracetamol, naproxen, diclofenac or flurbiprofen.

SPECIFIC COMPOUNDS

16 Compounds (I) are specifically claimed e.g:

1-(aminomethyl)cyclohexane acetic acid 2-methoxy-4-((1E)-3-(4-(nitrooxy)butoxy)-3-oxy-1-propenyl)phenyl hydrochloride ester (Ia).

To a solution of 1-(aminomethyl)cyclohexanacetic acid (10 g) in mixture of dioxane (100 ml) and water (150 ml), triethylamine (16.27 ml) and di-tert-butyl dicarbonate (15.3 g) were added. The reaction mixture was left at room temperature, under stirring for 4 hours and worked up to give 1-(N-tert-butoxycarbonylamino methyl)cyclohexanacetic acid (A). To a solution of ferulic acid (11.6 g) in tetrahydrofuran (400 ml), tetrabromomethane (39.62 g) and triphenylphosphine (31.34 g) were added. The obtained mixture was kept under stirring at room temperature for 5 hours, filtered, evaporated at reduced pressure and worked up to give 2-methoxy-4-((1E)-3-(4-(bromo)-butoxy)-3-oxy-1-propenyl)phenol. To a solution of this compound (8 g) in acetonitrile (500 ml), silver nitrate (12.25 g) was added. The reaction mixture was heated at 40°C for 12 hours sheltered from light and worked up to give 2-methoxy-4-((1E)-3-(4-(nitrooxy)butoxy)-3-oxy-1-propenyl)phenol (C1).

To a solution of (A) (2.5 g) in chloroform (200 ml) and N,N-dimethylformamide (3 ml), (C1) (3.15 g), dicyclohexylcarbodiimide (5.7 g) and N,N-dimethylaminopyridine (33 mg) were added. The reaction mixture was left at room temperature, under stirring for 3 hours and worked up to give 1-(N-tert-butoxycarbonylamino methyl)cyclohexanacetic acid 2-methoxy-4-((1E)-3-(4-(nitrooxy)butoxy)-3-oxy-1-propenyl)phenyl ester.

To a solution of this compound (5 g) in ethyl acetate (100 ml), a solution of 1N HCl in ethyl acetate (50 ml) was added. The reaction mixture was

left overnight at room temperature and concentrated under vacuum and worked up to give 1-(aminomethyl)cyclohexane acetic acid 2-methoxy-4-((1E)-3-(4-(nitrooxy)butoxy)-3-oxy-1-propenyl)phenyl hydrochloride ester (Ia) (1.8 g).

TITLE-TERMS: NEW DERIVATIVE TREAT EPILEPSY

DERWENT-CLASS: B05

CPI-CODES: B06-H; B07-H; B10-A03; B14-J07;

CHEMICAL-CODES: Chemical Indexing M2 *01*
Fragmentation Code C017 C100 C800
C801 C803 C804 C805 C806 C807 G015
G030 G038 G111 G563 H1 H100 H181
H5 H541 H7 H721 H8 J0 J012 J2 J241
J271 K0 K7 K710 M210 M211 M272
M281 M311 M312 M314 M321 M322 M332
M342 M372 M373 M383 M391 M392 M411
M510 M520 M531 M541 M640 M710 P442
Specific Compounds RA9QTR Registry
Numbers 673786

Chemical Indexing M2 *02*
Fragmentation Code C017 C100 C800
C801 C803 C804 C805 C806 C807 G012
G030 G038 G111 G563 H1 H100 H181
J0 J011 J2 J241 K0 K7 K710 M280
M311 M323 M342 M372 M373 M391 M392
M411 M510 M520 M531 M541 M640 M710
P442 Specific Compounds RA9QTU
Registry Numbers 673789

Chemical Indexing M2 *03*
Fragmentation Code H4 H498 H9 J0
J012 J2 J271 J3 J371 M210 M211
M213 M232 M262 M272 M281 M312 M321

M332 M343 M349 M381 M391 M416 M620
M710 P442 Specific Compounds
RA9R63 Registry Numbers 170395

Chemical Indexing M2 *04*
Fragmentation Code H1 H100 H181 H4
H498 H9 J0 J014 J1 J171 J2 J271 J3
J372 M210 M213 M232 M272 M281 M311
M312 M313 M321 M332 M342 M343 M349
M381 M393 M416 M620 M710 P442
Specific Compounds RA9R67 Registry
Numbers 96260

Chemical Indexing M2 *05*
Fragmentation Code C017 C100 C800
C801 C803 C804 C805 C806 C807 G012
G100 H1 H100 H181 J0 J011 J2 J241
K0 K7 K710 M280 M311 M314 M321
M331 M340 M342 M349 M373 M381 M391
M411 M510 M520 M531 M540 M640 M710
P442 Specific Compounds RA9QTV
Registry Numbers 673790

Chemical Indexing M2 *06*
Fragmentation Code C017 C100 C800
C801 C803 C804 C805 C806 C807 H1
H100 H181 J0 J012 J2 J272 J290 J3
J371 J9 K0 K7 K710 M210 M211 M262
M281 M312 M314 M321 M322 M331 M332
M340 M342 M343 M349 M381 M383 M391
M392 M411 M510 M520 M530 M540 M620
M640 M710 P442 Specific Compounds
RA9QTX Registry Numbers 673791

Chemical Indexing M2 *07*
Fragmentation Code C017 C100 C800
C801 C803 C804 C805 C806 C807 G030
G038 G563 H1 H100 H181 J0 J012 J2

J272 J290 J3 J371 J9 K0 K7 K710
M210 M211 M262 M281 M311 M312 M314
M321 M322 M332 M342 M343 M349 M372
M373 M381 M383 M391 M411 M510 M520
M530 M541 M640 M710 P442 Specific
Compounds RA9QTZ Registry Numbers
673795

Chemical Indexing M2 *08*
Fragmentation Code C017 C100 C800
C801 C803 C804 C805 C806 C807 F012
F016 F431 G030 G038 G563 H1 H100
H181 J0 J011 J2 J271 K0 K7 K710
M280 M311 M323 M342 M372 M373 M391
M393 M411 M510 M521 M530 M541 M640
M710 P442 Specific Compounds
RA9QU0 Registry Numbers 673797

Chemical Indexing M2 *09*
Fragmentation Code C017 C100 C800
C801 C803 C804 C805 C806 C807 G012
G100 H1 H100 H181 J0 J011 J2 J241
K0 K7 K710 L4 L420 M280 M311 M314
M321 M332 M342 M343 M349 M373 M381
M391 M411 M510 M520 M531 M540 M640
M710 P442 Specific Compounds
RA9QU1 Registry Numbers 673798

Chemical Indexing M2 *10*
Fragmentation Code C017 C100 C800
C801 C803 C804 C805 C806 C807 H1
H100 H181 J0 J012 J2 J272 J290 J3
J371 J9 K0 K7 K710 L4 L420 M210
M211 M262 M281 M312 M314 M321 M322
M332 M342 M343 M349 M381 M383 M391
M392 M411 M510 M520 M530 M540 M620
M640 M710 P442 Specific Compounds
RA9QU3 Registry Numbers 673800

Chemical Indexing M2 *11*
Fragmentation Code C017 C100 C800
C801 C803 C804 C805 C806 C807 G015
G100 H1 H100 H181 H5 H541 H7 H721
H8 J0 J012 J2 J241 J271 K0 K7 K710
L4 L420 M210 M211 M272 M281 M312
M314 M321 M322 M332 M342 M343 M349
M372 M381 M383 M391 M411 M510 M520
M531 M540 M640 M710 P442 Specific
Compounds RA9QU4 Registry Numbers
673801

Chemical Indexing M2 *12*
Fragmentation Code C017 C100 C800
C801 C803 C804 C805 C806 C807 G012
G100 H1 H100 H181 J0 J011 J2 J241
K0 K7 K710 L2 L250 M280 M311 M314
M321 M332 M342 M343 M349 M373 M381
M391 M411 M510 M520 M531 M540 M640
M710 P442 Specific Compounds
RA9QU5 Registry Numbers 673802

Chemical Indexing M2 *13*
Fragmentation Code C017 C100 C800
C801 C803 C804 C805 C806 C807 G015
G100 H1 H100 H181 H5 H541 H7 H721
H8 J0 J012 J2 J241 J271 K0 K7 K710
L2 L250 M210 M211 M272 M281 M312
M314 M321 M322 M332 M342 M343 M349
M372 M381 M383 M391 M411 M510 M520
M531 M540 M640 M710 P442 Specific
Compounds RA9QU6 Registry Numbers
673803

Chemical Indexing M2 *14*
Fragmentation Code C017 C100 C800
C801 C803 C804 C805 C806 C807 H1

H100 H181 J0 J012 J2 J272 J290 J3
J371 J9 K0 K7 K710 L2 L250 M210
M211 M262 M281 M312 M314 M321 M322
M332 M342 M343 M349 M381 M383 M391
M392 M411 M510 M520 M530 M540 M620
M640 M710 P442 Specific Compounds
RA9QU7 Registry Numbers 673804

Chemical Indexing M2 *15*
Fragmentation Code C017 C100 C800
C801 C803 C804 C805 C806 C807 G012
G100 J0 J011 J3 J331 K0 K7 K710 L2
L250 M280 M311 M314 M321 M332 M342
M373 M383 M391 M411 M510 M520 M531
M540 M640 M710 P442 Specific
Compounds RA9QU8 Registry Numbers
673805

Chemical Indexing M2 *16*
Fragmentation Code C116 F010 F011
F012 F014 F015 F020 F021 F140 F432
G001 G003 G010 G011 G012 G013 G015
G019 G050 G100 G111 G112 G113 G553
G563 H100 H101 H102 H103 H141 H181
H182 H201 H321 H341 H402 H442 H541
H600 H641 H642 H643 H685 H721 J011
J012 J013 J231 J271 J311 J331 J371
J5 J521 J581 J582 K351 K352 K353
K620 K640 K699 K710 K810 K830 K850
K899 L250 L410 L463 L640 L660 L699
L922 M121 M123 M129 M132 M135 M150
M210 M211 M212 M213 M214 M215 M216
M220 M221 M222 M223 M224 M225 M226
M231 M232 M233 M240 M262 M271 M272
M273 M280 M281 M282 M283 M311 M312
M313 M314 M315 M316 M320 M321 M322
M323 M331 M332 M333 M334 M340 M342
M343 M344 M349 M353 M371 M372 M373

M381 M382 M383 M391 M392 M393 M413
M414 M415 M416 M510 M520 M521 M522
M530 M531 M532 M533 M540 M541 M620
M630 M640 M650 M710 P442 Markush
Compounds 008706801

Chemical Indexing M2 *17*
Fragmentation Code H1 H100 H181 H4
H498 H9 J0 J014 J1 J171 J2 J271 J3
J372 M210 M213 M232 M272 M281 M311
M312 M313 M321 M332 M342 M343 M349
M381 M393 M416 M620 M710 P442
Specific Compounds RA9R66 Registry
Numbers 674340

Chemical Indexing M2 *18*
Fragmentation Code F011 F015 F521
H1 H100 H182 H2 H201 J0 J012 J1
J171 J3 J371 M210 M211 M273 M281
M312 M322 M332 M342 M343 M349 M371
M381 M391 M413 M510 M521 M530 M540
M710 M800 P442 Specific Compounds
R11742 Registry Numbers 87509

Chemical Indexing M2 *19*
Fragmentation Code B434 H1 H100
H181 H4 H498 H9 J0 J011 J1 J171
M280 M312 M321 M332 M343 M349 M381
M391 M411 M510 M520 M530 M540 M620
M710 P442 Specific Compounds
R07941 Registry Numbers 125177

Chemical Indexing M2 *20*
Fragmentation Code H1 H100 H181 H4
H498 H9 J0 J011 J1 J171 M280 M314
M321 M333 M343 M349 M381 M391 M416
M620 M710 P442 Specific Compounds
R00064 R22037 Registry Numbers

8198

Chemical Indexing M2 *21*
Fragmentation Code F011 F015 F521
H1 H100 H182 H2 H201 J0 J012 J2
J271 J3 J371 M210 M211 M212 M272
M273 M281 M312 M322 M332 M342 M343
M349 M371 M381 M391 M413 M510 M521
M530 M540 M710 P442 Specific
Compounds RA9R5N Registry Numbers
674321

Chemical Indexing M2 *22*
Fragmentation Code B434 H1 H100
H181 H5 H598 H9 J0 J011 J1 J171
M210 M211 M271 M281 M313 M321 M332
M343 M349 M381 M391 M411 M510 M520
M530 M540 M620 M710 P442 Specific
Compounds R06089 Registry Numbers
106864

Chemical Indexing M2 *23*
Fragmentation Code H1 H100 H181 H4
H498 H9 J0 J011 J1 J171 M280 M312
M321 M332 M343 M349 M381 M391 M416
M620 M710 P442 Specific Compounds
R01628 R12616 Registry Numbers
132396 141452 188253 2466 8188

Chemical Indexing M2 *24*
Fragmentation Code H4 H498 H9 J0
J012 J1 J171 J3 J371 M210 M211
M262 M281 M312 M321 M332 M343 M349
M381 M391 M416 M620 M710 P442
Specific Compounds R04369 Registry
Numbers 12143

Chemical Indexing M2 *25*

Fragmentation Code H1 H100 H181 H4
H498 H9 J0 J014 J1 J172 J3 J372
M280 M311 M312 M313 M321 M332 M342
M343 M349 M381 M393 M416 M620 M710
P442 Specific Compounds R00297
Registry Numbers 882

Chemical Indexing M2 *26*
Fragmentation Code G013 G100 H4
H401 H441 H7 H721 H8 J0 J011 J1
J171 M280 M312 M321 M332 M342 M372
M391 M414 M510 M520 M531 M540 M710
P442 Specific Compounds R01664
Registry Numbers 91684

Chemical Indexing M2 *27*
Fragmentation Code G015 G100 H4
H401 H441 H5 H541 H8 J0 J011 J1
J131 M210 M211 M272 M281 M320 M414
M510 M520 M531 M540 M710 P442
Specific Compounds R01012 Registry
Numbers 110027

Chemical Indexing M2 *28*
Fragmentation Code G015 G100 H4
H402 H442 H8 J0 J011 J1 J171 M280
M312 M321 M332 M342 M372 M391 M414
M510 M520 M531 M540 M710 P442
Specific Compounds RA03B0 Registry
Numbers 93147

Chemical Indexing M2 *29*
Fragmentation Code G015 G100 H4
H402 H442 H7 H721 H8 J0 J011 J1
J171 M280 M312 M321 M332 M342 M372
M391 M414 M510 M520 M531 M540 M710
P442 Specific Compounds R11260
Registry Numbers 89783

Chemical Indexing M2 *30*
Fragmentation Code H4 H401 H481 H8
J0 J013 J1 J173 M280 M313 M321
M332 M344 M349 M381 M391 M416 M620
M710 P442 Specific Compounds
R00419 R07029 Registry Numbers
104520 129792 129991 130395 132222
133510 140723 140725 159060 191428
2471 250717 278358 278359 3589 849
87079 95073 95095 99996

Chemical Indexing M2 *31*
Fragmentation Code G015 G100 H4
H402 H442 H8 J0 J011 J1 J131 M280
M320 M414 M510 M520 M531 M540 M710
P442 Specific Compounds R01283
Registry Numbers 96020

Chemical Indexing M2 *32*
Fragmentation Code G015 G100 H4
H401 H441 H5 H541 H7 H721 H8 J0
J011 J1 J171 M210 M211 M272 M281
M312 M321 M332 M342 M372 M391 M414
M510 M520 M531 M540 M710 P442
Specific Compounds R13076 Registry
Numbers 95106

Chemical Indexing M2 *33*
Fragmentation Code G017 G100 H4
H403 H443 H8 J0 J011 J1 J131 M280
M320 M414 M510 M520 M531 M540 M710
P442 Specific Compounds R01170
R09472 Registry Numbers 7650

Chemical Indexing M2 *34*
Fragmentation Code G015 G019 G100
H4 H404 H444 H8 M1 M121 M135 M280

M315 M321 M333 M342 M414 M510 M520
M532 M540 M710 P442 Specific
Compounds R06755 Registry Numbers
102281

Chemical Indexing M2 *35*
Fragmentation Code D014 D023 D120
G015 G100 H4 H404 H405 H421 H444
H8 J5 J521 J522 L9 L960 M1 M113
M280 M320 M412 M511 M520 M531 M540
M710 P442 Specific Compounds
R00971 RA0055 Registry Numbers
105172 129528

Chemical Indexing M2 *36*
Fragmentation Code D013 D023 D120
G015 G100 H4 H405 H421 H444 H8 M1
M113 M280 M320 M412 M511 M520 M531
M540 M710 P442 Specific Compounds
R04686 Registry Numbers 90953

Chemical Indexing M2 *37*
Fragmentation Code D014 D023 D120
G013 G100 H4 H403 H443 H8 J5 J522
L9 L960 M1 M113 M280 M320 M412
M511 M520 M531 M540 M710 P442
Specific Compounds R08510 Registry
Numbers 21764

Chemical Indexing M2 *38*
Fragmentation Code F012 F013 F014
F015 F113 H4 H403 H421 H482 H8 J5
J522 K0 L8 L818 L821 L832 L9 L942
L960 M280 M312 M321 M332 M343 M373
M391 M413 M510 M521 M530 M540 M710
P442 Specific Compounds R00035
R04454 Registry Numbers 185

Chemical Indexing M2 *39*
Fragmentation Code F012 F013 F014
F015 F017 F113 H4 H403 H421 H482
H8 J5 J522 K0 L8 L818 L821 L832 L9
L942 L960 M280 M312 M321 M332 M343
M373 M391 M413 M510 M521 M530 M540
M710 P442 Specific Compounds
R06288 R16366 Registry Numbers
98195

Chemical Indexing M2 *40*
Fragmentation Code G013 G100 H4
H402 H442 H8 M280 M320 M414 M510
M520 M531 M540 M710 P442 Specific
Compounds R01041 Registry Numbers
58

Chemical Indexing M2 *41*
Fragmentation Code G023 G024 G029
G221 G299 H4 H405 H444 H8 J4 J432
M1 M114 M210 M211 M213 M232 M240
M283 M320 M414 M510 M520 M532 M540
M710 P442 Specific Compounds
R11378 Registry Numbers 96388

Chemical Indexing M2 *42*
Fragmentation Code G036 G552 H4
H402 H462 H8 J5 J561 M280 M320
M415 M510 M520 M530 M541 M710 P442
Specific Compounds RA1YBQ Registry
Numbers 294262

Chemical Indexing M2 *43*
Fragmentation Code G015 G100 H4
H402 H442 H5 H541 H8 M210 M211
M272 M281 M320 M414 M510 M520 M531
M540 M710 P442 Specific Compounds
RA056K Registry Numbers 19087

Chemical Indexing M2 *44*
Fragmentation Code G015 G100 H4
H403 H443 H8 M280 M320 M414 M510
M520 M531 M540 M710 P442 Specific
Compounds R08208 Registry Numbers
23884

Chemical Indexing M2 *45*
Fragmentation Code G017 G100 H4
H403 H443 H8 J0 J011 J2 J231 M210
M213 M231 M272 M281 M320 M414 M510
M520 M531 M540 M710 P442 Specific
Compounds R04639 Registry Numbers
95847

Chemical Indexing M2 *46*
Fragmentation Code F012 F013 F014
F015 F016 F017 F019 F113 F123 H4
H405 H424 H483 H5 H521 H8 K0 L8
L814 L818 L822 L831 M1 M126 M141
M280 M311 M323 M342 M373 M393 M413
M510 M522 M530 M540 M710 P442
Specific Compounds R00135 Registry
Numbers 133509 2853

Chemical Indexing M2 *47*
Fragmentation Code C017 C100 C800
C801 C803 C804 C805 C806 C807 G030
G038 G563 H1 H100 H181 J0 J011 J2
J271 K0 K7 K710 M280 M311 M314
M321 M322 M332 M342 M372 M373 M383
M391 M411 M510 M520 M530 M541 M640
M710 P442 Specific Compounds
RA9QUA Registry Numbers 673807

Chemical Indexing M2 *48*
Fragmentation Code G013 G100 H4

H402 H441 H481 H7 H721 H8 M280
M313 M321 M332 M342 M373 M391 M414
M510 M520 M531 M540 M710 P442
Specific Compounds R11985 Registry
Numbers 141069

Chemical Indexing M2 *49*
Fragmentation Code G015 G100 H4
H402 H441 H481 H5 H541 H7 H721 H8
M210 M211 M272 M281 M313 M321 M332
M342 M373 M391 M414 M510 M520 M531
M540 M710 P442 Specific Compounds
R14887 Registry Numbers 8315

Chemical Indexing M2 *50*
Fragmentation Code G013 G100 H4
H402 H441 H481 H8 M280 M312 M321
M332 M342 M373 M391 M414 M510 M520
M531 M540 M710 P442 Specific
Compounds R14354 Registry Numbers
9344

Chemical Indexing M2 *51*
Fragmentation Code D011 D920 J5
J521 L9 L941 M280 M320 M412 M511
M520 M530 M540 M710 P442 Ring
Index Numbers 01174 Specific
Compounds R01218 R04867 Registry
Numbers 86977

Chemical Indexing M2 *52*
Fragmentation Code H5 H598 H9 J0
J012 J1 J172 M280 M312 M322 M332
M342 M381 M392 M416 M620 M710 P442
Specific Compounds R05349 Registry
Numbers 108778

Chemical Indexing M2 *53*

Fragmentation Code H4 H401 H481 H8
J0 J012 J1 J172 J5 J581 K0 L5 L560
M280 M311 M321 M343 M349 M381 M391
M416 M620 M710 P442 Specific
Compounds R13040 Registry Numbers
69951

Chemical Indexing M2 *54*
Fragmentation Code H7 H721 J0 J012
J1 J172 M280 M312 M321 M332 M342
M382 M391 M416 M710 P442 Specific
Compounds R00902 R04891 Registry
Numbers 130347 132553 134096
134238 143998 205770 205776 232427
7658

Chemical Indexing M2 *55*
Fragmentation Code C017 C100 C800
C801 C803 C804 C805 C806 C807 G015
G100 H5 H541 H7 H721 H8 J0 J012 J2
J241 J3 J371 K0 K7 K710 L2 L250
M210 M211 M272 M281 M312 M313 M314
M321 M332 M342 M372 M381 M383 M391
M411 M510 M520 M531 M540 M640 M710
P442 Specific Compounds RA9QUB
Registry Numbers 673808

Chemical Indexing M2 *56*
Fragmentation Code G017 G100 H4
H401 H441 H498 H8 H9 J0 J011 J2
J271 M210 M214 M233 M240 M282 M311
M322 M342 M349 M373 M381 M391 M414
M510 M520 M531 M540 M710 P442
Specific Compounds RA9R5G Registry
Numbers 674315

Chemical Indexing M2 *57*
Fragmentation Code F014 F521 H1

H100 H181 J0 J012 J2 J271 J3 J371
M210 M212 M272 M281 M312 M322 M332
M342 M343 M349 M371 M381 M391 M413
M510 M521 M530 M540 M710 P442
Specific Compounds RA9R5J Registry
Numbers 674317

Chemical Indexing M2 *58*
Fragmentation Code F014 F521 H1
H100 H181 J0 J012 J2 J271 J3 J371
M210 M213 M232 M272 M281 M312 M322
M332 M342 M343 M349 M371 M381 M391
M413 M510 M521 M530 M540 M710 P442
Specific Compounds RA9R5K Registry
Numbers 674318

Chemical Indexing M2 *59*
Fragmentation Code F011 F015 F521
H1 H100 H182 H2 H201 J0 J012 J2
J271 J3 J371 M210 M211 M213 M232
M272 M273 M281 M312 M322 M332 M342
M343 M349 M371 M381 M391 M413 M510
M521 M530 M540 M710 P442 Specific
Compounds RA9R5O Registry Numbers
674322

Chemical Indexing M2 *60*
Fragmentation Code B434 H1 H100
H181 H4 H498 H9 J0 J011 J2 J271
M210 M212 M272 M281 M312 M321 M332
M343 M349 M381 M391 M411 M510 M520
M530 M540 M620 M710 P442 Specific
Compounds RA9R5R Registry Numbers
674325

Chemical Indexing M2 *61*
Fragmentation Code B434 H1 H100
H181 H4 H498 H9 J0 J011 J2 J271

M210 M213 M232 M272 M281 M312 M321
M332 M343 M349 M381 M391 M411 M510
M520 M530 M540 M620 M710 P442
Specific Compounds RA9R5S Registry
Numbers 674327

Chemical Indexing M2 *62*
Fragmentation Code B434 H1 H100
H181 H5 H598 H9 J0 J011 J2 J271
M210 M211 M212 M271 M272 M281 M313
M321 M332 M343 M349 M381 M391 M411
M510 M520 M530 M540 M620 M710 P442
Specific Compounds RA9R5U Registry
Numbers 674329

Chemical Indexing M2 *63*
Fragmentation Code H1 H100 H181 H4
H498 H9 J0 J011 J2 J271 M210 M212
M272 M281 M314 M321 M333 M343 M349
M381 M391 M416 M620 M710 P442
Specific Compounds RA9R5Y Registry
Numbers 674704

Chemical Indexing M2 *64*
Fragmentation Code B434 H1 H100
H181 H5 H598 H9 J0 J011 J2 J271
M210 M211 M213 M232 M271 M272 M281
M313 M321 M332 M343 M349 M381 M391
M411 M510 M520 M530 M540 M620 M710
P442 Specific Compounds RA9R5W
Registry Numbers 674331

Chemical Indexing M2 *65*
Fragmentation Code H4 H498 H9 J0
J012 J2 J271 J3 J371 M210 M211
M212 M262 M272 M281 M314 M321 M333
M343 M349 M381 M391 M416 M620 M710
P442 Specific Compounds RA9R60

Registry Numbers 674706

Chemical Indexing M2 *66*

Fragmentation Code H1 H100 H181 H4
H498 H9 J0 J011 J2 J271 M210 M213
M232 M272 M281 M314 M321 M333 M343
M349 M381 M391 M416 M620 M710 P442
Specific Compounds RA9R5Z Registry
Numbers 674334

Chemical Indexing M2 *67*

Fragmentation Code H4 H498 H9 J0
J012 J2 J271 J3 J371 M210 M211
M212 M262 M272 M281 M312 M321 M332
M343 M349 M381 M391 M416 M620 M710
P442 Specific Compounds RA4DPH
Registry Numbers 411706

Chemical Indexing M2 *68*

Fragmentation Code H4 H498 H9 J0
J012 J1 J171 J3 J371 M210 M211
M262 M281 M314 M321 M333 M343 M349
M381 M391 M416 M620 M710 P442
Specific Compounds RA24WX Registry
Numbers 86396

Chemical Indexing M2 *69*

Fragmentation Code H1 H100 H181 H4
H498 H9 J0 J011 J2 J271 M210 M213
M232 M272 M281 M312 M321 M332 M343
M349 M381 M391 M416 M620 M710 P442
Specific Compounds RA5ZNK Registry
Numbers 92121

Chemical Indexing M2 *70*

Fragmentation Code H1 H100 H181 H4
H498 H9 J0 J011 J2 J271 M210 M212
M272 M281 M312 M321 M332 M343 M349

M381 M391 M416 M620 M710 P442
Specific Compounds RA30IJ Registry
Numbers 92120

Chemical Indexing M2 *71*
Fragmentation Code H1 H103 H182 J0
J014 J1 J173 M280 M311 M312 M321
M323 M332 M342 M349 M381 M383 M391
M393 M416 M620 M710 P442 Specific
Compounds R00195 R04870 Registry
Numbers 129933 130071 130946
131585 132742 133268 3330 4238
5021 591 93951 93962

Chemical Indexing M2 *72*
Fragmentation Code H4 H498 H9 J0
J012 J2 J271 J3 J371 M210 M211
M213 M232 M262 M272 M281 M314 M321
M333 M343 M349 M381 M391 M416 M620
M710 P442 Specific Compounds
RA9R61 Registry Numbers 674336

Chemical Indexing M2 *73*
Fragmentation Code H1 H100 H181 H4
H498 H9 J0 J014 J1 J171 J2 J271 J3
J372 M210 M212 M272 M281 M311 M312
M313 M321 M332 M342 M343 M349 M381
M393 M416 M620 M710 P442 Specific
Compounds RA9R65 Registry Numbers
674339

Chemical Indexing M2 *74*
Fragmentation Code H1 H100 H181 H4
H498 H9 J0 J014 J1 J171 J2 J271 J3
J372 M210 M212 M272 M281 M311 M312
M313 M321 M332 M342 M343 M349 M381
M393 M416 M620 M710 P442 Specific
Compounds RA3ITX Registry Numbers

96259

Chemical Indexing M2 *75*
Fragmentation Code F014 F521 H1
H100 H181 J0 J012 J1 J171 J3 J371
M280 M312 M322 M332 M342 M343 M349
M371 M381 M391 M413 M510 M521 M530
M540 M710 P442 Specific Compounds
R08807 Registry Numbers 90096

UNLINKED-DERWENT-REGISTRY- ; 0035U ; 0035S ;
NUMBERS : 0064U ; 0064S ;
0135U ; 0135S ;
0195U ; 0195S ;
0297U ; 0297S ;
0419U ; 0419S ;
0902U ; 0902S ;
0971U ; 0971S ;
1012U ; 1012S ;
1041U ; 1041S ;
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